Technical and Bibliographic Notes / Notes techniques et bibliographiques

The Institute has attempted to obtain the best original copy available for filming. Features of this copy which may be bibliographically unique, which may alter any of the images in the reproduction, or which may significantly change the usual method of filming, are checked below.

L'Institut a microfilmé le meilleur exemplaire qu'il lui a été possible de se procurer. Les détails de cet exemplaire qui sont peut-être uniques du point de vue bibliographique, qui peuvent modifier une image reproduite, ou qui peuvent exiger une modification dans la méthode normale de filmage sont indiqués ci-dessous.

- [x] Coloured covers/ Couverture de couleur
- [ ] Covers damaged/ Couverture endommagée
- [ ] Covers restored and/or laminated/ Couverture restaurée et/ou pelliculée
- [ ] Cover title missing/ Le titre de couverture manque
- [ ] Coloured maps/ Cartes géographiques en couleur
- [ ] Coloured ink (i.e. other than blue or black)/ Encre de couleur (i.e. autre que bleue ou noire)
- [ ] Coloured plates and/or illustrations/ Planches et/ou illustrations en couleur
- [ ] ınd with other material/ : avec d'autres documents
- [x] Tight binding may cause shadows or distortion along interior margin/ La reliure serrée peut causer de l'ombre ou de la distorsion le long de la marge intérieure
- [ ] Blank leaves added during restoration may appear within the text. Whenever possible, these have been omitted from filming/ Il se peut que certaines pages blanches ajoutées lors d'une restauration apparaissent dans le texte, mais, lorsque cela était possible, ces pages n'ont pas été filmées.

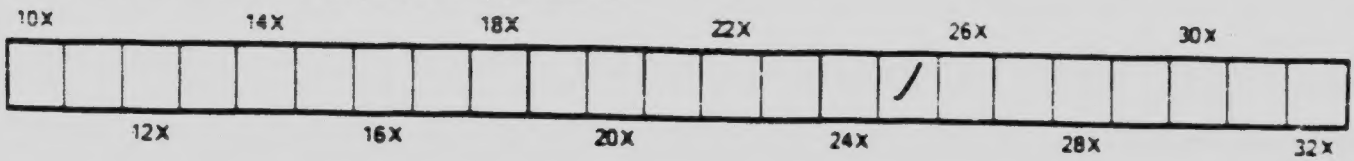
- [ ] Coloured pages/ Pages de couleur
- [ ] Pages damaged/ Pages endommagées
- [ ] Pages restored and/or laminated/ Pages restaurées et/ou pelliculées
- [x] Pages discoloured, stained or foxed/ Pages décolorées, tachetées ou piquées
- [ ] Pages detached/ Pages détachées
- [x] Showthrough/ Transparence
- [ ] Quality of print varies/ Qualité inégale de l'impression
- [ ] Continuous pagination/ Pagination continue
- [ ] Includes index(es)/ Comprend un (des) index

  Title on header taken from:/ Le titre de l'en-tête provient:

- [ ] Title page of issue/ Page de titre de la livraison
- [ ] Caption of issue/ Titre de départ de la livraison
- [ ] Masthead/ Générique (périodiques) de la livraison

- [x] Additional comments:/ Commentaires supplémentaires: Pagination is as follows : p. 51-62.

This item is filmed at the reduction ratio checked below/
Ce document est filmé au taux de réduction indiqué ci-dessous.



UNIVERSITY OF TORONTO
STUDIES

PHYSIOLOGICAL SERIES

No. 11: THE COMPARATIVE VALUE OF LARD AND BUTTER IN GROWTH. BY CASIMIR FUNK and ARCHIBALD BRUCE MACALLUM

(REPRINTED FROM THE JOURNAL OF BIOLOGICAL CHEMISTRY, VOL. XXVII.)

THE UNIVERSITY LIBRARY: PUBLISHED BY
THE LIBRARIAN, 1916

Reprinted from THE JOURNAL OF BIOLOGICAL CHEMISTRY, Vol. XXVII, No. 1, 1916

STUDIES ON GROWTH.

III. THE COMPARATIVE VALUE OF LARD AND BUTTER FAT IN GROWTH.

By CASIMIR FUNK AND ARCHIBALD BRUCE MACALLUM.*

(From the General Memorial Hospital, Harriman Research Laboratory, Roosevelt Hospital, New York, and the Department of Pathological Chemistry, University of Toronto.)

(Received for publication, August 3, 1916.)

In our first communication[1] of this series, we advanced the opinion that we were dealing with a problem very similar to, if not identical with, beri-beri. Our main objective was to ascertain the simplest dietary conditions necessary to enable a young rat to reach maturity. Subsequently we found[2] that artificial diets containing butter, without yeast or similar vitamine-containing substances, are insufficient to promote growth in young rats; and at that time the question whether butter could be replaced by lard with the same ultimate success was left open. We have carried out experiments of longer duration, employing both lard and butter as the fat fraction of these diets, and submit results which enable us to form a more definite opinion as to the relative value of these two fats.

Our experience demonstrates that there are wide variations depending on the constitution of the individual rats. Every rat taken indiscriminately is not suitable for this class of work. As a matter of fact in experiments carried out in Toronto 80 per cent of the rats purchased from dealers were rejected on account of physical defects not apparent before the initiation of the experiment. A second complication is a diminished resistance to infection, which follows the use of all artificial diets. The meager knowledge we possess of the pathological conditions

* Senior Fellow in Medical Research.

[1] Funk, C., and Macallum, A. B., Jr., *Z. physiol. Chem.*, 1914, xcii, 13.

[2] Funk and Macallum, *J. Biol. Chem.*, 1915, xxiii, 413.

in rats may lead to a condemnation of the diet; whereas actually the condition could be remedied without change of diet, if we were able to recognize its nature. As an example of this, rats on artificial diets frequently contract an eye infection which can be treated with a certain degree of success by an application of a few drops of zinc sulfate solution. If untreated this condition is accompanied by loss in weight, becomes acute, and terminates fatally.

The first series of experiments were carried out on diets containing lard as the fat component, and dried powdered yeast. Rats on this diet grew normally for 60 to 90 days, but eventually displayed symptoms (bleeding from the eyes, nose, and ears, petechiæ and hemorrhages under the skin of the tail) which might be regarded as scorbutic. This terminated fatally if no change of diet was effected. When moist yeast was substituted for the dried preparation the rats could be kept for 150 days and attained approximately adult size. Autolyzed yeast was equally efficient in this respect. Similar results were obtained on addition of orange juice to the drinking water, although orange juice itself has neither growth-promoting nor maintaining properties, unless supplemented by yeast.

Diets in which butter partially or wholly replaces lard have a slight superiority over those containing lard, which is more than can be explained by the antiscorbutic properties of the butter. Rats on yeast and butter diets often show the eye affection regarded by most of the investigators as characteristic of dietary deficiencies, and we are convinced that none of the artificial diets so far investigated can be compared with a normal dietary in its efficiency for growth. This deficiency introduces an additional complication and must be taken into account in subsequent investigations.

EXPERIMENTAL.

The methods of preparing the diets were very much the same as those described in our earlier publications. The experiments varied slightly as to their conditions in New York and Toronto but the ultimate results were identical. The charts and tables are representative of the different groups of experiments.

Experiment I.

Rats 49, 50, 51, and 52 (Fig. 1) were kept on diets containing dried yeast and lard for about 68 days. At that time a deficiency was noticed which, in previous experiments, led to the death of all the rats and could not be corrected by a larger supply of dried yeast. Then fresh moist pressed yeast was substituted, the deficiency disappeared, and the rats attained approximately adult weight.

A second series, Rats 61 and 62 (Fig. 2), were placed on diets containing lard for 44 days, being changed to a diet of butter and dried yeast after this period. No increment in growth was noticed as the result of this change.

In the butter experiments Rats 53 and 54 (Fig. 1) have also shown a marked improvement on changing the yeast from the dried to the moist form, more especially as regards their external appearance. Rats 47 and 48 (Fig. 2) were kept on diets with butter and dried yeast and these have also developed symptoms which persisted when the diets were substituted by lard and autolyzed yeast. Rats 59 and 60 (Fig. 2), exceptionally healthy specimens, were kept on butter-containing diet for 44 days and then changed[3] to diet with lard and autolyzed yeast, for a longer period than was indicated in the chart, without the rate of growth being modified. On several occasions rats showing deficiency on a lard-containing diet were placed on a butter diet with the hope of relieving the symptoms. The improvement which resulted from this change was only temporary and several rats died after being kept 30 days on butter.

In all the experiments a marked improvement resulted when a diet of a different composition was given or even from a fresh preparation of the same diet. This might indicate that the diets lose part of their nutritive value when stored for lengthy periods.

[3] Encircled numbers on Fig. 2 indicate the point at which that diet was begun.

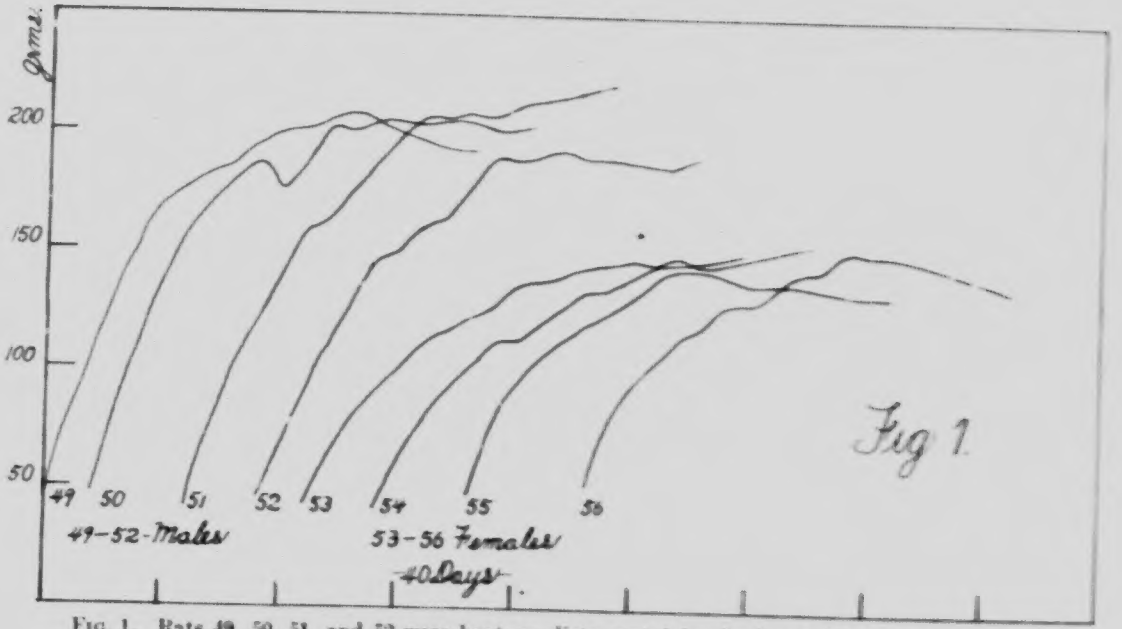
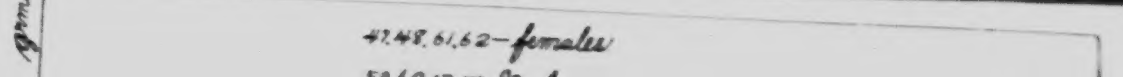


FIG. 1. Rats 49, 50, 51, and 52 were kept on diets containing lard and dried yeast. The animals recovered when moist yeast was substituted for dried yeast. Rats 53 and 54 were kept on butter and dried yeast. Here also a marked recovery was noticed on changing to the wet form of yeast. Rats 55 and 56 were kept on a diet containing casein purified according to the method of McCollum; no advantage of the use of this method is noticeable.



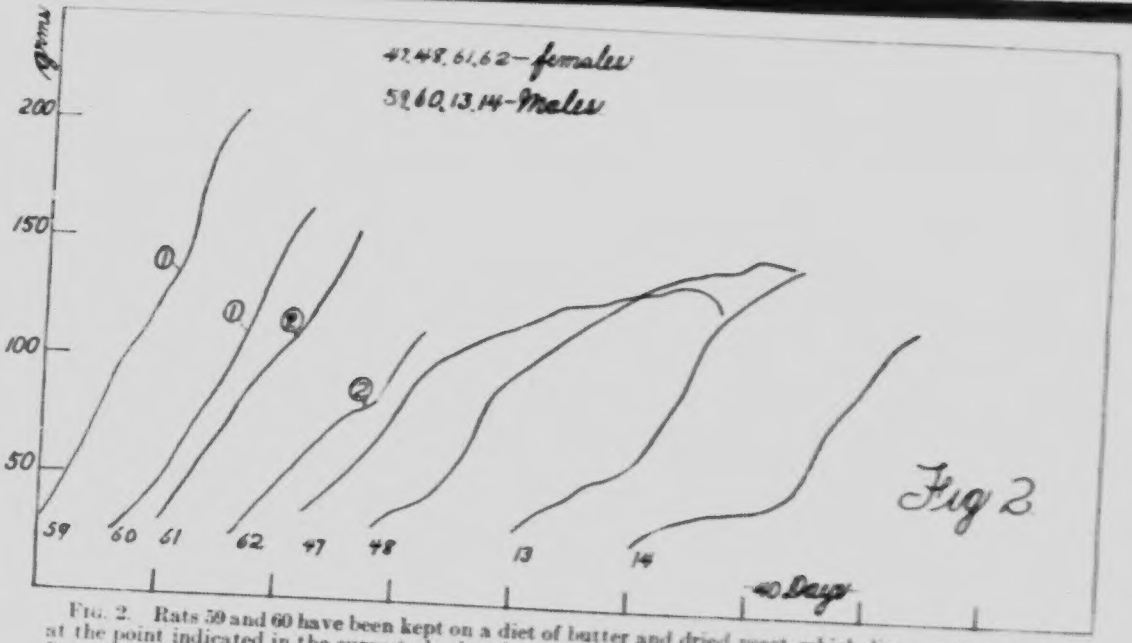


FIG. 2. Rats 59 and 60 have been kept on a diet of butter and dried yeast, which diet was then changed at the point indicated in the curve to lard and autolyzed yeast without any effect on the rate of growth. Rats 61 and 62 were kept on lard and then changed to butter without any effect on growth. Rats 47 and 48 were kept on butter and dried yeast and developed signs of food deficiency which persisted when the diet was changed to lard and autolyzed yeast. Rats 13 and 14 were kept on a diet containing casein which had been autoclaved. The rats failed to grow on this diet but recovered when 1 cc. of orange juice was added, which indicates that this deficiency was not due to chemical changes in the casein.

Diets (Gm.).

	1.	2.	3.	4.	5.
Casein	22	22	22	22	22
Sugar	10	10	10	10	10
Starch	30	27	27	29	27
Lard	30	30	30	30	30
Salt	3	3	6	6	6
Agar	2	2	2	2	2
Yeast (dry)	3	6	3		
Yeast (moist) equal to				1 of dry yeast.	3 of dry yeast

Rats 49 and 50. Males.
0- 68 days Diet 2
69- 98 " " 4
99–150 " " 5

Rats 51 and 52. Males.
0- 52 days Diet 1
53- 68 " " 3
69- 98 " " 4
99–150 " " 5

Days.	Weight.		Average food intake per day.	Weight.		Average food intake per day.
	49.	50.		51.	52.	
	gm.	*gm.*	*calories*	*gm.*	*gm.*	*calories*
0	44	46		41	46	
4	55	58	77.4	62	55	78.2
8	81	85	92.4	72	65	81.3
12	96	100	103.2	91	82	67.2
16	104	110	105.7	102	91	97.1
20	119	124	110.3	110	100	102.2
24	132	137	110.5	119	110	106.8
28	146	150	110.0	132	120	100.3
32	150	158	111.0	138	128	100.8
36	162	163	109.3	148	138	112.2
40	170	174	114.6	159	147	116.2
44	173	176	114.3	160	150	115.2
48	177	180	111.1	163	150	117.5
52	178	184	95.4	170	158	108.6
56	182	188	110.8	176	161	120.3
60	185	191	103.8	178	163	106.6
64	186	176	78.7	175	164	96.9
68	184	182	90.0	192	167	120.7
76	199	200	115.9			116.3
84	201	201	98.5	206	199	108.5
100	207	205	85.0	209	192	91.0
120	200	205	105.7	210	199	103.7
140	193	201	76.3	216	186	85.4
150	192	203	75.8	221	199	67.4

Diets (Gm.).

	1.	2.	3.	4.
Casein	22	22	22	22
Sugar	10	10	10	10
Starch	30	27	29	27
Butter fat	18	18	18	18
Lard	12	12	12	12
Salt	3	3	6	6
Agar	2	2	2	2
Yeast (dry)	3	6		
Yeast (moist) equal to			1 of dry yeast.	3 of dry yeast.

Rats 53 and 54. Females.
0–52 days Diet 1
53–68 " " 2
69–100 " " 3
101–150 " " 4

Days.	Weight.		Average daily food intake.
	53.	54.	
	gm.	*gm.*	*calories*
0	43	41	
4	54	55	74.3
8	64	63	66.2
12	78	75	72.0
16	80	80	77.0
20	85	87	73.5
24	90	92	76.8
28	96	95	81.1
32	100	101	79.2
36	106	106	88.9
40	112	112	87.3
48	112	112	87.2
56	119	116	83.7
64	123	126	95.2
84	138	135	79.8
100	144	146	76.5
120	149	147	79.2
150	147	153	92.8

Diets (Gm.)

	1	2.	3
Casein	22	22	22
Sugar	10	10	10
Starch	28	30	23
Butter	30	30	
Lard			30
Agar	2	2	2
Salts	2	2	2
$NaHCO_3$	1	1	1
Yeast (dry)		3	
Yeast (autolyzed) equal to	1.5 of dry yeast.		3 of dry yeast.

Rats 47 and 48. Females.
0– 16 days Diet 1.
16–123 " " 2.
123–140 " " 3.

Days.	Weight.		Average daily food intake.
	47.	48.	
	gm.	*gm.*	*gm.*
0	36 5	31	
4	41	34	6 2
8	45.5	39	9.5
12	51 5	43	9.1
16	54.5	42 5	9.1
20	58	45	10.0
24	67 5	50.5	11.2
28	76	56.5	12.1
32	85	66	14.1
36	91	78	13.6
40	99	91	14.2
44	102	93	12.5
48	105	98	13.5
52	108	100.5	14.5
56	111	107	14.3
60	114.5	113.5	15.0
64	115.5	115	16.9
68	119	122	15.2
72	119	120	14.0
76	121.5	125.5	15 3
80	124.5	129.5	15.3
84	127	134.5	17.1
88	128	134.5	14.6
92	126.5	135	14.1
96	128 5	139	16.1
100	130 5	141	14.7
108	134	144 5	16.6
116	133	145	16.9
124	135	146.5	16.6
132	139.5	154	14 6
140	128	149 5	14 0

Diets (Gm.).

	1.	2.
Casein	22	22
Starch	23	30
Sugar	10	10
Butter		30
Lard	30	
Agar	2	2
Salts	2	2
$NaHCO_3$	1	1
Yeast (dry)		3
Yeast (autolyzed) equal to	3 of dry yeast.	

Rats 59 and 60. Males.
0–44 days Diet 2.
45–64 " " 1.

Rats 61 and 62. Females.
0–44 days Diet 1.
45–64 " " 2.

Days.	Weight.		Average daily food intake	Days.	Weight.		Average daily food intake.
	59.	60.			61.	62.	
	gm.	gm	gm.		gm.	gm.	gm.
0	30.5	25	6.7	0	30.5	25.5	6 6
4	40	31	8 2	4	38	32	9 3
8	47 5	35.5	9 7	8	46 5	38	9 3
12	59	42.5	11 2	12	55.5	43	10 7
16	70	48	13 8	16	62 5	48	12 5
20	81.5	58.5	14 8	20	71.5	55	12.6
24	94	68	16 2	24	80.5	61.5	14.6
28	106	75.5	17.2	28	87.5	67	14 2
32	114	82.5	20.1	32	93.5	71	16.1
36	127.5	90	20 8	36	99.5	76	14.9
40	139.5	100.5	23 8	40	105	80 5	14.2
44	155	113	24 9	44	111.5	84.5	14.2
48	167	124	23 7	48	115	83	16 6
52	180	138	21.8	52	123	96	17 6
56	192	150	22.0	56	132	100	15 2
60	199	157	21.1	60	142	104.5	17 1
64	205	165	21.1	64	156 5	115	

Experiment II.

The casein preparation used in this series was purified by washing, following the method of McCollum and Davis.[4] In

[4] McCollum, E. V., and Davis, M., *J. Biol. Chem.*, 1915, xxiii. 231.

this paper the authors claim that purification of casein by boiling with alcohol destroys some of the amino-acids and results in loss of its nutritive properties. The results in this case (Rats 55 and 56, Fig. 1) were identical with those which were obtained with casein purified by extraction with hot alcohol. This latter method was used in purifying the casein in the first experiment.

Diets (Gm.).

	1.	2.	3.
Casein (McCollum)	22	22	22
Sugar	10	10	10
Starch	27	29	27
Lard	30	30	30
Salt	3	6	6
Agar	2	2	2
Yeast (dry)	6		
Yeast (moist) equal to		1 of dry yeast.	3 of dry yeast

Rats 55 and 56. Females.
0– 59 days Diet 1.
60– 87 " " 2.
88–140 " " 3.

Days.	Weight.		Average daily food intake.
	55.	56.	
	gm.	*gm.*	*calories*
0	48	52	
4	67	71	75.1
8	80	82	92.2
12	89	91	88.4
16	96	96	77.2
20	104	102	86.0
24	107	104	74.9
28	109	109	64.3
32	115	116	79.8
40	120	120	88.4
60	140	133	86.3
80	144	143	78.4
100	136	150	79.9
140	133	136	61.9

Another series, of which Rats 13 and 14 (Fig. 2) are representatives, received casein which had been autoclaved for 1 hour at 15 pounds' pressure, according to McCollum and Davis. On this diet the rats failed to grow, but after 28 days 1 cc. of fresh orange juice was added, and normal growth was resumed. It seems probable that the impaired value of heated casein is not due so much to the destruction of amino-acids as to the loss of its anti-scorbutic properties.

Diets (Gm.)

	1.	2.
Casein	22	22
Sugar	10	10
Starch	30	29
Lard	30	30
Salts	3	3
Agar	2	2
Yeast (dry)	3	4

Rats 13 and 14. Males.
0– 14 days Diet 1.
15– 96 " " 2.
28–100 " 1 cc. orange juice.

Days.	Weight.		Average daily food intake.
	13.	14.	
	gm.	gm.	gm.
0	33.3	27.2	
4	40.1	33.7	6.2
8	41.4	37.1	6.0
12	44.6	39.8	7.1
16	46.4	39.4	7.9
20	50.6	41.4	7.2
24	54.3	42.0	8.1
28	54.6	41.5	6.5
32	55.1	42.0	4.7
36	63.1	47.0	8.2
40	62.1	44.0	6.8
44	70.8	46.2	8.4
48	77.1	46.2	10.6
52	87.1	51.8	12.2

Rats 13 and 14. Males—*Continued.*

Days.	Weight.		Average daily food intake.
	13.	14.	
	gm.	*gm.*	*gm.*
56	93.0	54.6	12.4
60	102.0	64.2	12.9
64	119.3	78.6	15.6
68	126.0	89.3	15.1
72	130.0	91.6	15.4
76	130.9	98.6	14.9
80	137.4	103.8	15.1
84	140.0	112.4	14.8
88	144.7	117.0	11.2
92	145.0	119.8	14.2
96	147.0	123.0	11.4

SUMMARY.

The failure of rats to grow on a lard and yeast diet is partially due to the development of scorbutic symptoms. These can be relieved to a marked degree by using moist instead of dried yeast and still more so by using moist yeast and butter. Even in the latter case the existing deficiencies are not entirely corrected, since many rats decline on this diet. Rats which fail on lard do not always recover on a diet containing butter. It seems also possible that yeast on account of its high content in purines, and perhaps other constituents, is not an ideal addition in experiments of long duration, even in spite of its marked growth-promoting power. The impaired nutritive value of heated casein does not seem to be due to destruction of amino-acids but to destruction of vitamines.

UNIVERSITY OF TORONTO STUDIES

Physiological Series

No. 1: The structure, micro-chemistry and development of nerve-cells, with special reference to their nuclein compounds, by F. H. Scott 0.50

No. 2: On the cytology of non-nucleated organisms, by A. B. Macallum 0.75

No. 3: Observations on blood pressure, by R. D. Rudolf . . . 0.75

No. 4: The chemistry of wheat gluten, by G. G. Nasmith . . . 0.50

No. 5: The palaeochemistry of the ocean, by A. B. Macallum 0.25

No. 6: The absorption of fat in the intestine, by G. E. Wilson 0.50

No. 7: The distribution of fat, chlorides, phosphates, potassium and iron in striated muscle, by Mary L. Menten 0.25

No. 8: Surface tension and vital phenomena, by A. B. Macallum 1.00

No. 9: On the distribution of potassium in renal cells, by C. P. Brown 0.25

No. 10: On the probable nature of the substance promoting growth in young animals, by Casimir Funk and A. Bruce Macallum 0.25

No. 11: The comparative value of lard and butter in growth, by Casimir Funk and A. Bruce Macallum. 0.25

No. 12: The action of yeast fractions on the growth of rats, by Casimir Funk and A. Bruce Macallum 0.25

No. 13: A new conception of the glomerular function, by T. G. Brodie 1.00
On changes in the glomeruli and tubules of the kidney accompanying activity, by T. G. Brodie and J. J. Mackenzie 1.00

No. 14: Further observations on the differential action of adrenalin, by Frank A. Hartman and Lois McPhedran . . . 0.50

No. 15: The mechanism for vasodilatation from adrenalin, by Frank A. Hartman and Lois McPhedran Fraser 0.50